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EXAMINER	
CHEN, S	
ART UNIT	**PAPER NUMBER**
1633	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/984,900	Anthony J.F. D'Apice et al.
Examiner	**Group Art Unit**
Shin-Lin Chen	1633

Responsive to communication(s) filed on _____.

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- [X] Claim(s) *1-3, 46-51, 67, and 68* is/are pending in the application.
- Of the above, claim(s) _____ is/are withdrawn from consideration.
- [ ] Claim(s) _____ is/are allowed.
- [X] Claim(s) *1-3, 46-51, 67, and 68* is/are rejected.
- [ ] Claim(s) _____ is/are objected to.
- [ ] Claims _____ are subject to restriction or election requirement.

Application Papers

- [ ] See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.
- [ ] The proposed drawing correction, filed on _____ is [ ] approved [ ] disapproved.
- [ ] The specification is objected to by the Examiner.
- [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
  - [ ] All [ ] Some* [ ] None of the CERTIFIED copies of the priority documents have been
    - [ ] received.
    - [ ] received in Application No. (Series Code/Serial Number) _____.
    - [ ] received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - *Certified copies not received: _____
- Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- [X] Notice of References Cited, PTO-892
- [ ] Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- [ ] Interview Summary, PTO-413
- [ ] Notice of Draftsperson's Patent Drawing Review, PTO-948
- [ ] Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

This is application is a continuation of Application No. 08/378,617 which was filed on 1-26-95, issued as US Patent No. 5,849,991, which is a continuation-in-part of Application No. 08/188,607 filed on 1-27-94, abandoned on 7-1-95. Applicants claimed priority of the filing date 1-26-95 of Application No. 08/378,617.

The amendment filed 8-30-99 (Paper No. 13) has been entered. Claims 52-66 have been canceled. Claim 1 has been amended. Claim 68 has been added. Claims 1-3, 46-51, 67 and 68 are pending.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

2. Claims 1-3 and 68 are rejected under 35 U.S.C. 102(e) as being anticipated by Sandrin et al.,1998, US Patent No. 5,821,117 (A). Claim 68 is newly added claim. Claim 1 has been amended. Applicant submits amendment to the specification (Paper No. 13) and claims priority of US Application No. 08/188,607 filed 1-27-94.

Claims 1-3 and 68 are directed to nucleic acid molecule comprising SEQ ID No.7, SEQ ID No.7 within the scope of the degeneracy of the genetic code, sequences encoding porcine α-1,3 galactosyltransferase (α-1,3GT) and that hybridize to SEQ ID No.7 under high stringency condition, host cell transformed with said nucleic acid and a porcine α-1,3 GT encoded by said nucleic acid. Sandrin et al. publishes a porcine α-1,3 galactosyltransferase cDNA sequence (SEQ ID No.2) which is 98.9% homologous (from base 108-1335) to base 185-1412 of SEQ ID No.7 of the present application and will hybridize to SEQ ID No.7 under high stringency condition. Sandrin et al. also disclosed a λgt11 cDNA library expressing porcine α-1,3 GT in a host cell for the isolation of the porcine α-1,3,GT cDNA (e.g. column 9, 10). Thus, claims 1-3 and 68 are anticipated by Sandrin et al..

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 46-51 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sandrin et al., US Patent 5,821,117 (A) and Galili, 1993 (U). Claim 1 has been amended.

Applicant submits amendment to the specification (Paper No. 13) and claims priority of US Application No. 08/188,607 filed 1-27-94.

Claims 46-51 and 67 are drawn to DNA construct comprising a disrupted porcine α-1,3 galactosyltransferase (α-1,3,GT) gene, wherein the disruption is by the insertion of an exogenous sequence such as neo^R gene or hyg^R gene within exon 4, 7, 8, or exon 9 of the porcine α-1,3,GT gene, or the exogenous sequence is flanked at its 5' and 3' ends by FRT DNA elements; a method of generating a porcine cell comprising at least one inactivated α-1,3 galactosyltransferase gene by introducing said DNA construct into porcine cells such that homologous recombination occurs between chromosome sequence and DNA construct; a porcine cell comprising at least one inactivated α-1,3 GT gene.

Sandrin et al., which have priority date on 3-16-93, revealed a porcine α-1,3 galactosyltransferase cDNA sequence (SEQ ID No.2) which is 98.9% homologous (from base 108-1335) to base 185-1412 of SEQ ID No.7 of the present application and disclosed a λgt11 cDNA library expressing porcine α-1,3 GT in a host cell for the isolation of the porcine α-1,3,GT cDNA. Sandrin et al. discussed the hyperacute rejection in xenotransplantation, particularly in the context of pig tissue, is associated with antibodies reactive with galactose in an α-1,3 linkage with galactose, and teach a method of inhibiting xenotransplant rejection in an animal patient by introducing mutants of nucleotide sequences in a vector such as plasmid, viral vector encoding α-1,3 GT into embryonic stem cells via homologous recombination for the inactivation of wild type

α-1,3 GT genes, wherein the mutant α-1,3 GT nucleotide sequences include nucleotide deletions, insertions, substitutions and additions to wild type α-1,3 GT gene such that the resultant mutant does not encode functional galactosyl transferase. Sandrin et al. also teach the vectors encoding a-1,3 GT may include restriction sites for the insertion of additional genes and/or selection markers, as well as elements necessary for the propagation and maintenance of vectors within cells (e.g. column 1, 3, 9, 10).

Galili discussed that the immunological barrier by anti-Gal interacting with α-galactosyl epitopes on the discordant graft cells might be difficult to overcome by means of immunosuppression, and suggested the use of xenografts devoid of α-galactosyl epitopes obtained from nonprimate donors which are genetically engineered to lack α-1,3 GT activity by gene knockout technology or by the production of transgenic animals with anti-sense DNA to the α-1,3 GT gene.

Sandrin et al. and Galili do not teach introducing the exogenous sequence within exon 4, 7, 8, or exon 9 of the porcine α-1,3,GT gene, or using the exogenous sequence flanked at its 5' and 3' ends by FRT DNA elements. Introducing the exogenous sequence within exon 4, 7, 8, or exon 9 of the porcine α-1,3,GT gene are all for the purpose of interrupting α-1,3 GT gene which results in non-functional α-1,3,GT, and using the exogenous sequence flanked at its 5' and 3' ends by FRT DNA elements is to facilitate the homologous recombination between the exogenous sequence and chromosome genome. Both are well known in the art and are obvious for a person of ordinary skill at the time of the invention. Thus, it would have been prima facie

obvious for a person of ordinary skill at the time of invention to have made a DNA construct comprising a disrupted α-1,3 galactosyltransferase, a porcine cell comprising at least one inactivated α-1,3 galactosyltransferase via homologous recombination with reasonable expectation of success. Therefore, claims 46-51 and 67 are rejected under 35 U.S.C 103(a).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Stanton can be reached on (703) 308-2801. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

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Shin-Lin Chen, Ph.D.

BRUCE R. CAMPELL
PRIMARY EXAMINER
GROUP 1800